

REMARKS

Traversal of Examiner's Section 102(b)  
Rejection of Claims 1 to 3 and 6 as Being Anticipated by WO 92/15686

The Examiner rejected Claims 1 to 3 and 6 under Section 102(b) as being anticipated by WO 92/15686. According to the Examiner, Examples 1 to 3 of the '686 publication disclose a substance formed by anydridizing the active serine residue of blood coagulation factor VII.

The Examiner's rejection of Claims 2 and 3 has been rendered moot by the cancellation of such claims.

With respect to Claims 1 and 6, applicant submits respectfully that the Examiner is in error by characterizing the modified factor VII compound of the '686 publication as having an anhydridized serine. Rather, the compound of the '686 publication was formed by the complete substitution of the active site serine of factor VII with alanine. Alanine is not anhydridized serine. Since Claim 1 recites that the substance comprise an anhydridized active site serine and Claim 6 is dependent therefrom, the '686 publication does not teach each element of the rejected claims and, therefore, does not anticipate such claims.

Furthermore, by teaching the complete replacement of the active site serine, the '686 publication teaches against the compounds of the present invention having anhydridized active serine residues. Claims 1 and 6 are, therefore, also not obvious in view of the '686 publication under Section 103(a).

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Given the above, applicant requests respectfully the withdrawal of the Examiner's rejection of Claims 1 and 6 as being anticipated by the '686 publication.

Traversal of Examiner's Section 102(b)

Rejection of Claims 1 to 5 and 8 as Being Anticipated by U.S. Patent No. 5,679,639

The Examiner rejected Claims 1 to 5 and 8 under Section 102(b) as being anticipated by U.S. Patent No. 5,679,639. According to the Examiner, the '639 patent discloses factor IX and factor X molecules which have been modified so that they now serve as inhibitors of factor IX and factor X activity, respectively.

The Examiner's rejection of Claims 2 and 3 have been rendered moot by the cancellation of such claims.

With respect to Claims 1, 4, 5, and 8, applicant submits respectfully that the Examiner is in error. Claim 1, on which Claims 4 and 5 depend, and Claim 8, which include the recitations thereof, recite that the substance comprises an anhydridized active site serine. Nowhere in the '639 patent is there any disclosure of a compound which comprises an anhydridized active site serine. The '639 patent thus does not teach each element of the rejected claims and, therefore, does not anticipate such claims.

The '639 patent does not even remotely suggest anhydridizing active serine resides. Claims 1, 4, 5 and 8 are, therefore, also not obvious in view of the '639 patent.

Given the above, applicant requests respectfully the withdrawal of the Examiner's rejection of Claims 1, 4, 5, and 8 as being anticipated by the '639 patent.

**Traversal of Examiner's Section 102(b)**  
Rejection of Claim 7 as Being Anticipated by Skogen et al.

The Examiner rejected Claim 7 under Section 102(b) as being anticipated by Skogen et al., *J. Biol. Chem.*, 259: 2306-10 (1984). According to the Examiner, Skogen et al. teaches a method for modifying activated factor X using synthetic inhibitor PMSF.

Claim 7, in addition to reciting the reaction of a compound with PMSF, recites alkali treatment of the compound at pH 11.0-13.5 and the use of a polyhydric alcohol and/or saccharine in combination with a salt or an amphoteric electrolyte. Skogen et al. does not disclose alkali treatment of a compound at pH 11.0-13.5 or the use of polyhydric alcohol and/or saccharine in combination with a salt or an amphoteric electrolyte. These last two elements are important as alkali treatment allows for the synthetic inhibitor (e.g., PMSF) to be dissociated from the remainder of the compound and the combined use of polyhydric alcohol and/or saccharide with a salt or an amphoteric electrolite can promote anhydridization and also effect regeneration of the compound without inducing coagulation and association thereof. As Skogen et al. does not teach these elements, it fails to anticipate Claim 7.

Furthermore, by omitting entirely so many elements Skogen et al. fails to even remotely suggest the subject matter of claim 7. Claim 7 therefore also patentably defines over Skogen et al. under Section 103(a).

Given the above, applicant requests respectfully the withdrawal of the Examiner's rejection of Claim 7 as being anticipated by Skogen et al.

**Traversal of the Examiner's Rejection of Claims 1 to 6 and 8  
Under the Written Description Requirement of Section 112, First Paragraph**

The Examiner rejected Claims 1 to 6 and 8 under the written description requirement of Section 112, first paragraph, because, according to the Examiner, the descriptive portion of the application does not adequately support such claims. According to the Examiner, the claimed substance is not adequately described structurally and the application includes only a few examples of such a substance, namely anhydridized activated factor X, anhydridized activated factor IX, and anhydridized activated factor VII.

The Examiner's rejection of Claims 2 and 3 have been rendered moot by the cancellation of such claims.

With respect to Claims 1, 4 to 6, and 8, applicant notes that Claim 1, from which Claims 3 to 6 depend and Claim 8 includes the recitations thereof, has been amended to recite that the substance be an activated blood coagulation factor containing an anhydridized active serine residue wherein the activated blood coagulation factor is activated blood coagulation factor X, activated blood coagulation factor IX, or activated blood coagulation factor VII. Accordingly, there is significant structural information respecting the substance within the claims. Further, as the Examiner himself noted, such compounds are exemplified in the descriptive portion of the application (see Examples 1 to 3).

Given the above, applicant requests respectfully the withdrawal of the Examiner's rejection of Claims 1 to 6 and 8 under the written description requirement of Section 112, first paragraph.

**Traversal of the Examiner's Rejection of Claim 7  
Under the Written Description Requirement of Section 112, First Paragraph**

The Examiner rejected Claim 7 under the written description requirement of Section 112, first paragraph, because, according to the Examiner, the descriptive portion of the application does not describe the method claimed. According to the Examiner, Examples 1 to 3 describe a method for making the subject substance but fails to teach each of the steps of the claimed method.

Applicant submits respectfully that the Examiner is in error. It appears that the Examiner believes that Examples 1 to 3 describe the reaction of the blood factor with PMSF at pH 7 to 8 whereas, according to the Examiner, the claims recite the reaction of the blood factor with PMSF at pH 11.0-13.5. It should be clarified that the reaction of the blood factor with PMSF and the alkali treatment of the product at pH 11.0-13.5, as described in the claims, are two separate steps. Examples 1 to 3 do indeed exemplify these two separate steps as well as the third "collection" step. In Example 1 to 3, the reaction of activated factor X with PMSF is described in the first full paragraph after the title, whereas the alkali treatment step is described in the second full paragraph. It is only after the alkali treatment step that the pH is adjusted to pH 8. The remaining portions of the above Examples describes the third "collection" step. A more general description of the method is provided in the application on pages 9 to 15.

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Given the above, there exists abundant description of the claimed method. Applicant accordingly requests the withdrawal of the Examiner's rejection of Claim 7 under the written description requirement of Section 112, first paragraph.

Conclusion

For the reasons expressed above, applicants request respectfully that the Examiner reconsider and withdraw the rejections under §§102 and 112.

In view of the foregoing amendment and remarks, an early and favorable action is requested respectfully.

Respectfully submitted,



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